

AMENDMENTS

In the Claims

Please amend the claims as follows:

1-91. (Cancelled)

92. (Currently amended) An in vivo method of delivering a pharmaceutical composition to a target polynucleotide comprising administering to the airways of a subject said pharmaceutical composition of a respirable or inhalable particle size of about 0.5 μm to about 10 μm in size or 10 μm to 500 μm in size comprising ~~a nucleic acid that comprises~~ at least one antisense oligonucleotide effective to alleviate hyper-responsiveness to adenosine or increased levels of adenosine, or to alleviate bronchoconstriction, asthma, or lung allergy, wherein the oligonucleotide is 7 to 60 nucleotides long and comprises ~~up to about 15%~~ or less adenosine.

93. (Currently amended) The method of claim 92, wherein the antisense oligonucleotide comprises ~~up to about 10%~~ or less adenosine.

94. (Currently amended) The method of claim 93, wherein the antisense oligonucleotide comprises ~~up to about 5%~~ or less adenosine.

95. (Currently amended) The method of claim 94, wherein the antisense oligonucleotide comprises ~~up to about 2%~~ or less adenosine.

96. (Currently amended) The method of claim 95, wherein the antisense oligonucleotide is adenosine-free.

97. (Currently amended) The method of claim 92, wherein the antisense oligonucleotide is 10 to 36 nucleotides long.

98. (Currently amended) The method of claim 97, wherein the antisense oligonucleotide is 12 or 21 nucleotides long.

99. (Previously presented) The method of claim 92, wherein the pharmaceutical composition is administered by inhalation directly to the airway or lung of the subject.

100. (Currently amended) The method of claim 92, wherein the antisense oligonucleotide is antisense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a target polypeptide associated with pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, cystic fibrosis, allergic rhinitis, pulmonary hypertension, emphysema, chronic obstructive pulmonary disease, bronchitis, and lung cancer, or is antisense to the corresponding mRNA thereof.

101. (Currently amended) The method of claim 92, wherein the particle size is ~~about~~ 0.5 μm to ~~about~~ 10 μm in size.

102. (Previously presented) The method of claim 101, wherein the particle size is 10 μm to 500 μm in size.

103. (Previously presented) The method of claim 92, wherein the pharmaceutical composition further comprises a surfactant.

104. (Previously presented) The method of claim 92, wherein the hyper-responsiveness to adenosine, hyper-responsiveness to increased levels of adenosine, hyper-responsiveness to increased levels of an adenosine receptor, bronchoconstriction, asthma, lung allergy, or lung inflammation is associated with pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, cystic fibrosis, allergic rhinitis, pulmonary hypertension, emphysema, chronic obstructive pulmonary disease, bronchitis, and lung cancer.

105. (Currently amended) The method of claim 92, wherein the ~~nucleic acid~~ antisense oligonucleotide is administered in an amount of about 0.01 to about 150 mg/kg body weight.

106. (Previously presented) The method of claim 92, wherein said method is a prophylactic or therapeutic method.

107. (Currently amended) The method of claim 92, wherein the antisense oligonucleotide is antisense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding bradykinin B2 receptor.

108. (Currently amended) The method of claim 92, wherein the antisense oligonucleotide comprises at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, 3'-thioformacetal, triformacetal, carbamate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methylimino), methyleneoxy (methylimino), methoxyethyl, C₅-substituted nucleotide and methyloxyethyl.

109. (Currently amended) A pharmaceutical composition comprising a ~~nucleic acid~~ that comprises at least one antisense oligonucleotide that is antisense to a target polynucleotide and when delivered to the airways of a subject is effective to alleviate hyper-responsiveness to adenosine or increased levels of adenosine, or to alleviate bronchoconstriction, asthma, or lung allergy, wherein the oligonucleotide is 7 to 60 nucleotides long and comprises ~~up to about 15% or less~~ adenosine, wherein said pharmaceutical composition is of a respirable or inhalable particle size of about 0.5 μ m to about 10 μ m in size or 10 μ m to 500 μ m in size.

110. (Currently amended) The pharmaceutical composition of claim 109, wherein the antisense oligonucleotide comprises ~~up to about 10% or less~~ adenosine.

111. (Currently amended) The pharmaceutical composition of claim 110, wherein the antisense oligonucleotide comprises ~~up to about 5% or less~~ adenosine.

112. (Currently amended) The pharmaceutical composition of claim 111, wherein the

antisense oligonucleotide comprises ~~up to about~~ 2% or less adenosine.

113. (Currently amended) The pharmaceutical composition of claim 112, wherein the antisense oligonucleotide is adenosine-free.

114. (Currently amended) The pharmaceutical composition of claim 109, wherein the antisense oligonucleotide is 10 to 36 nucleotides long.

115. (Currently amended) The pharmaceutical composition of claim 114, wherein the antisense oligonucleotide is 12 or 21 nucleotides long.

116. (Previously presented) The pharmaceutical composition of claim 109, wherein the pharmaceutical composition is delivered by inhalation directly to the airway or lung of the subject.

117. (Currently amended) The pharmaceutical composition of claim 109, wherein the antisense oligonucleotide is antisense to the initiation codon, the coding region or the 5' or 3' intron-exon junction of a target polypeptide associated with pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, cystic fibrosis, allergic rhinitis, pulmonary hypertension, emphysema, chronic obstructive pulmonary disease, bronchitis, and lung cancer, or is antisense to the corresponding mRNA thereof.

118. (Currently amended) The pharmaceutical composition of claim 109, wherein the particle size is ~~about~~ 0.5 μm to about 10 μm in size.

119. (Previously presented) The pharmaceutical composition of claim 109, wherein the particle size is 10 μm to 500 μm in size.

120. (Previously presented) The pharmaceutical composition of claim 109, wherein the pharmaceutical composition further comprises a surfactant.

121. (Previously presented) The pharmaceutical composition of claim 109, wherein the

hyper-responsiveness to adenosine, hyper-responsiveness to increased levels of adenosine, hyper-responsiveness to increased levels of an adenosine receptor, bronchoconstriction, asthma, lung allergy, or lung inflammation is associated with pulmonary vasoconstriction, inflammation, allergies, asthma, impeded respiration, respiratory distress syndrome, cystic fibrosis, allergic rhinitis, pulmonary hypertension, emphysema, chronic obstructive pulmonary disease, bronchitis, and lung cancer.

122. (Currently amended) The pharmaceutical composition of claim 109, wherein the nucleic acid antisense oligonucleotide is delivered in an amount of about 0.01 to about 150 mg/kg body weight.

123. (Previously presented) The pharmaceutical composition of claim 109, wherein the delivery of said pharmaceutical composition is prophylactic or therapeutic.

124. (Currently amended) The pharmaceutical composition of claim 109, wherein the antisense oligonucleotide is antisense to the initiation codon, the coding region or the 5' or 3' intron-exon junctions of a gene encoding bradykinin B2 receptor.

125. (Currently amended) The pharmaceutical composition of claim 109, wherein the antisense oligonucleotide comprises at least one mononucleotide is linked or modified by one or more of phosphorothioate, phosphorodithioate, methylphosphonate, phosphoramidate, boranophosphate, 3'-thioformacetal, triformacetal, carbamate, phosphotriester, formacetal, 2'-O-methyl, thioformacetal, 5'-thioether, carbonate, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene (methyylimino), methyleneoxy (methyylimino), methoxyethyl, C₅-substituted nucleotide and methyloxyethyl.